Claims

1. An isolated nucleic acid comprising a nucleotide sequence encoding a polypeptide wherein: (a) the polypeptide comprises (i) an Sp35 LRR domain, (ii) an Sp35 basic region C-terminal to the LRR domain, and (iii) an Sp 35 immunoglobulin (Ig) domain C-terminal to the basic region; and (b) the polypeptide lacks a transmembrane domain.

2. An isolated nucleic acid comprising a nucleotide sequence encoding a polypeptide wherein the polypeptide comprises an Sp35 Ig domain and lacks an Sp35 LRR domain, an Sp35 basic region, a transmembrane domain, and a cytoplasmic domain.

3. An isolated nucleic acid comprising a nucleotide sequence encoding a polypeptide wherein the polypeptide comprises an Sp35 LRR domain and lacks an Sp35 Ig domain, an Sp35 basic region, a transmembrane domain, and a cytoplasmic domain.

4. The nucleic acid of claim 1, wherein the Sp35 polypeptide lacks a cytoplasmic domain.

5. The nucleic acid of claim 1, wherein the polypeptide comprises amino acid residues 34-532 of SEQ ID NO: 2.

6. The nucleic acid of any one of claims 1-3, wherein the polypeptide is a fusion polypeptide comprising a non-Sp35 moiety.

7. The nucleic acid of claim 6, wherein the non-Sp35 moiety is selected from the group consisting of an Ig moiety, a serum albumin moiety, a targeting moiety, a reporter moiety, and a purification-facilitating moiety.

8. The nucleic acid of claim 7, wherein the non-Sp35 moiety is an Ig moiety.

9. The nucleic acid of claim 8, wherein the Ig moiety is an Fc moiety.

10. The nucleic acid of any one of claims 1-3, wherein the nucleotide sequence is operatively linked to an expression control sequence.

11. A vector comprising the nucleic acid of claim 10.

12. A host cell comprising the vector of claim 11.

13. An isolated polypeptide, wherein: (a) the polypeptide comprises (i) an Sp35 LRR domain, (ii) an Sp35 basic region C-terminal to the LRR domain, and (iii) an immunoglobulin (Ig) domain C-terminal to the basic region; and (b) the polypeptide lacks a transmembrane domain.

14. An isolated polypeptide wherein the polypeptide comprises an Sp35 Ig domain and lacks an LRR domain, an Sp35 basic region, a transmembrane domain, and a cytoplasmic domain.

15. An isolated polypeptide wherein the polypeptide comprises an Sp35 LRR domain and lacks an Sp35 Ig domain, an Sp35 basic region, a transmembrane domain, and a cytoplasmic domain.

16. The polypeptide of claim 13, wherein one of the leucine rich repeats is a carboxy-terminal leucine-rich repeat (LRRCT).

17. The polypeptide of claim 13, wherein one of the leucine rich repeats is an amino-terminal leucine-rich repeat (LRRNT).

18. The polypeptide of claim 13, wherein the Sp35 polypeptide lacks a cytoplasmic domain.

19. The polypeptide of claim 13, wherein the polypeptide comprises amino acid residues 34-532 of SEQ ID NO: 2.

20. The polypeptide of claim 13, 14 or 15, wherein the polypeptide is a fusion polypeptide comprising a non-Sp35 moiety.

21. The polypeptide of claim 20, wherein the non-Sp35 moiety is selected from the group consisting of an Ig moiety, a serum albumin moiety, a targeting moiety, a reporter moiety, and a purification-facilitating moiety.

22. The polypeptide of claim 21, wherein the non-Sp35 moiety is an Ig moiety.

23. The polypeptide of claim 22, wherein the Ig moiety is an Fc moiety.

24. The polypeptide of claim 13, 14 or 15, wherein the polypeptide is conjugated to a polymer.

25. The polypeptide of claim 24, wherein the polymer is selected from the group consisting of a polyalkylene glycol, a sugar polymer, and a polypeptide.

26. The polypeptide of claim 25, wherein the polymer is a polyalkylene glycol.

27. The polypeptide of claim 26, wherein the polyalkylene glycol is polyethylene glycol (PEG).

28. The polypeptide of claim 24, wherein the polypeptide is conjugated to 1, 2, 3 or 4 polymers.

29. The polypeptide of claim 28, wherein the total molecular weight of the polymers is from 20,000 Da to 40,000 Da.

30. A method of inhibiting signal transduction by NgR1, comprising contacting the NgR1 with an effective amount of an Sp35 polypeptide.

31. A method of decreasing inhibition of axonal growth of a central nervous system (CNS) neuron, comprising contacting the neuron with an effective amount of a polypeptide selected from the group consisting of an Sp35 polypeptide, an anti-Sp35 antibody, or an antigen-binding fragment of an anti-Sp35 antibody.

32. A method of inhibiting growth cone collapse of a CNS neuron, comprising contacting the neuron with an effective amount of a polypeptide selected from the group consisting of an Sp35 polypeptide, an anti-Sp35 antibody, or an antigen-binding fragment of an anti-Sp35 antibody.

33. A method of treating a CNS disease, disorder or injury in a mammal, comprising administering to the mammal a therapeutically effective amount of a polypeptide selected from the group consisting of an Sp35 polypeptide, an anti-Sp35 antibody, or an antigen-binding fragment of an anti-Sp35 antibody.

34. The method of any one of claims 30-33, wherein the Sp35 polypeptide is selected from the group consisting of

a polypeptide, wherein: (a) the polypeptide comprises (i) an LRR domain comprising 12-14 Sp35 leucine-rich repeats, (ii) an Sp35 basic region C-terminal to the LRR domain, and (iii) an immunoglobulin (Ig) domain C-terminal to the basic region; and (b) the polypeptide lacks a transmembrane domain; and

a polypeptide wherein the polypeptide comprises an Sp35 Ig domain and lacks an LRR domain, a basic region, a transmembrane domain, and a cytoplasmic domain.

35. The method of claim 33, wherein the CNS disease, disorder or injury is a spinal cord injury or an optic nerve injury.

36. The method of claim 33, wherein the polypeptide is administered locally.

37. The method of claim 33, wherein the polypeptide is administered initially within 48 hours of the spinal cord injury.

38. The method of claim 36, wherein the therapeutically effective amount of the polypeptide is from 10 μg to 10 mg.

39. A method of treating a CNS disease, disorder or injury in a mammal, comprising (a) providing a cultured host cell expressing a recombinant Sp35 polypeptide; and (b) introducing the host cell into the mammal at or near the site of the CNS disease, disorder or injury.

40. The method of claim 39, wherein the disease, disorder or injury is a spinal cord injury.

41. The method of claim 39, wherein the cultured host cell is derived from the mammal to be treated.

42. The method of claim 39, wherein the recombinant Sp35 polypeptide is a full-length Sp35 polypeptide.

43. A method of promoting myelination at the site of the CNS disease, disorder or injury, comprising contacting the site of the CNS disease, disorder or injury with an effective amount of an Sp35 polypeptide.

44. The method of claim 43, wherein the Sp35 polypeptide comprises an Sp35 LRR domain and lacks an Sp35 Ig domain, an Sp35 basic region, a transmembrane domain, and a cytoplasmic domain.

45. A method of treating a CNS disease, disorder or injury by *in vivo* gene therapy, comprising administering to a mammal, at or near the site of the disease, disorder or injury, a viral vector comprising a nucleotide sequence that encodes an Sp35 polypeptide so that the Sp35 polypeptide is expressed from the nucleotide sequence in the mammal in an amount sufficient to reduce inhibition of axonal extension by neurons at or near the site of the injury.

46. The method of claim 36, wherein the viral vector is selected from the group consisting of an adenoviral vector, a lentiviral vector, a baculoviral vector, an Epstein Barr viral vector, a papovaviral vector, a vaccinia viral vector, and a herpes simplex viral vector.

47. The method of claim 45, wherein the disease, disorder or injury is selected from the group consisting of spinal cord injury and optic nerve injury.

48. The method of claim 45, wherein the viral vector is administered by a route selected from the group consisting of topical administration, intraocular administration, parenteral administration, intrathecal administration, subdural administration and subcutaneous administration.

49. A nucleic acid encoding a polypeptide comprising an Sp35 LRR domain, basic region, Ig domain, connecting sequence, and transmembrane domain; and lacking a functional cytoplasmic domain.

50. The nucleic acid of claim 49, wherein the nucleic acid encodes a polypeptide consisting essentially of amino acids 1-576 of SEQ ID NO: 2.

51. A method of promoting survival of a neuron at risk of dying, comprising contacting the neuron with an effective amount of an Sp35 polypeptide.

52. The method of claim 51, wherein the neuron is *in vitro*.

53. The method of claim 51, wherein the neuron is in a mammal with a neurodegenerative disease disorder or injury.

54. The method of claim 53, wherein the neurodegenerative disease, disorder or injury is selected from the group consisting of multiple sclerosis, ALS, Huntington's disease, Alzheimer's disease, Parkinson's disease, diabetic neuropathy, stroke, traumatic brain injuries and spinal cord injury.

55. A method of promoting survival of a neuron at risk of death of dying in a mammal with a neurodegenerative disease, disorder or injury, comprising (a) providing a cultured host cell expressing a recombinant Sp35 polypeptide; and (b) introducing the host cell into the mammal at the site of the neuron.

56. An *in vivo* gene therapy method of promoting survival of a neuron at risk of dying, comprising administering to a mammal, at or near the site of the neuron, a viral vector comprising a nucleotide sequence that encodes an Sp35 polypeptide so that the Sp35 polypeptide is expressed from the nucleotide sequence in the mammal in an amount sufficient to promote survival of the neuron.

57. The method of claim 51, wherein the Sp35 polypeptide is soluble.